510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
k033940

B. Analyte:
Amoxicillin/Clavulanate Potassium at 0.25/0.12-128/64ug/mL AST

C. Type of Test:
Quantitative growth based detection algorithm using optics light detection

D. Applicant:
Dade Behring Inc.
Dade MicroScan Inc.

E. Proprietary and Established Names:
Dried Gram-Negative MIC/Combo panels

F. Regulatory Information:

1. Regulation section:
   866.1640 Antimicrobial Susceptibility Test Powder
2. Classification:
   II
3. Product Code:
   LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems
   JWY - Manual Antimicrobial Susceptibility Test Systems
   LTT – Panels, Test, Susceptibility, Antimicrobial
   LTW – Susceptibility Test Cards, Antimicrobial
4. Panel:
   83 Microbiology

G. Intended Use:

1. Intended use(s):
   For use with MicroScan® Dried Gram Negative MIC/Combo Panels and Dried Gram Negative Breakpoint Combo Panels.
   MicroScan® panels are designed for use in determining antimicrobial agent susceptibility and/or identification to the species level of aerobic and facultatively anaerobic gram-negative bacilli.

   The MicroScan® Dried Gram-Negative MIC/Combo Panel is used to determine quantitative and/or qualitative antimicrobial agent susceptibility of

colonies grown on solid media of rapidly growing aerobic and facultative anaerobic gram-negative bacilli.

2. Indication(s) for use:
   This will include the antibiotic Amoxicillin/Clavulanate Potassium at 0.25/0.12-128/64ug/mL for testing the appropriate organism in the *Enterobacteriaceae* group.
3. Special condition for use statement(s):
   The Prompt™ method of inoculation is an alternate method of inoculum preparation that is supported in the product insert along with the turbidity method. The stationary and log inoculum methods should not be used with this antibiotic.
4. Special instrument Requirements:
   These panels can be read at ≥ 16 hours of incubation either manually, automatically on the autoSCAN® 4, or with the WalkAway® instrument systems.

H. Device Description:

The MicroScan® Dried Gram-Negative MIC/Combo Panel contains microdilutions of each antimicrobial agent in various concentrations with Mueller Hinton Broth and various nutrients which are dehydrated and dried in panels. Each panel contains two control wells: a no-growth control well (contains water only/no nutrients or broth), and a growth control well (contains test medium without antibiotic). The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the turbidity method (inoculum prepared in water, then 0.1ml transferred to 25ml of inoculum water containing pluronic-D/F-a wetting solution). The Prompt™ method of inoculation is also recommended as an alternate means of preparing the inoculum. The panels are incubated at 35^{o} C in a non-CO_2 incubator for 16-20 hours and read by visual observation for growth. Panels may also be read automatically with the WalkAway® or the AutoSCAN®4.

I. Substantial Equivalence Information:

1. Predicate device name(s):
   MicroScan® Dried Gram-Negative and Gram-Positive MIC/Combo Panels
2. Predicate K number(s):
   K862140
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended Use	For use with MicroScan® Dried Gram Negative MIC/Combo Panels and Dried Gram Negative Breakpoint Combo Panels. MicroScan® panels are designed for use in determining antimicrobial agent susceptibility and/or identification to the species level of aerobic and facultatively	Same

	anaerobic gram-negative bacilli.	
Test Panel	Dried	same
Instrument/manual	Both manual and instrument reading available.	same
Technology	Growth based after 16 hours incubation	same
Results	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR).	Same

Differences

Item	Device	Predicate
Reading algorithm	Unique for Amoxicillin/ Clavulanate Potassium	Unique for each antibiotic
Test organism	*Enterobacteriaceae*	Gram positive and gram negative organisms
Inoculum preparation from colonies	Turbidity and Prompt™	All methods recommended in the package insert.

J. Standard/Guidance Document Referenced (if applicable):

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA"; NCCLS M7 (M100-S13) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard".

K. Test Principle:

After incubation in a non-CO_2 incubator for 16-20 hours, the minimum inhibitory concentration (MIC) for the test organisms are read by determining the lowest antimicrobial concentration showing inhibition of growth. The panels are read either manually using a touchSCAN® SR, or with the autoSCAN 4® or the WalkAway® instrument, which uses an optics systems with growth algorithms to directly measure organism growth.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was demonstrated using 10 isolates tested at 3 sites on 3 separate days in triplicate. All ten isolates had a mode that was on scale. The study included the testing of the following inoculum and reading variables; turbidity inoculum method and Prompt™ method of inoculation with reading performed manually using a touchSCAN® SR, or by instrumentation using the autoSCAN 4® or the WalkAway® instrument. The following table provides the overall reproducibility results for all combinations of these variables:

Difference in the number of dilutions between the mode of the MicroScan result and the actual result with each different variable for overall reproducibility							
Inoculation method	Read method	≥ Minus 2 dilutions	Minus 1 dilution	Exact	Plus 1 dilution	≥ Plus 2 dilutions	% repro-ducible
Turbidity	Manual(touchSCAN ®)		16	209	38	6	97.8
Turbidity	WalkAway ®		4	221	38	7	97.4
Turbidity	autoSCAN® 4		14	208	41	7	97.4
Prompt™	Manual(touchSCAN ®)		31	225	12	2	99.3
Prompt™	WalkAway ®		22	234	12	2	99.3
Prompt™	autoSCAN® 4		11	226	31	2	99.3

This demonstrates good reproducibility overall but the Turbidity method also had one site that was reproducible at <95% (within site reproducibility) for all read methods.

The reproducibility strains were also evaluated for inoculum density for the Prompt™ method with colony counts ranging from 1 x 10^5 to 13 x 10^5 with the same variability that was noticed in the Quality Control inoculum density studies. Also more of the averages tended to be closer to 1 x 10^6 than those that were closer to 5 x 10^5.

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b. Linearity/assay reportable range:
Not applicable

c. Traceability (controls, calibrators, or method):

Quality Control was performed daily with the turbidity method and with the Prompt™ selectively with the following results.

ORGANISM			**RESULTS**					
	ug/mL	ref	Turbidity inoculation			Prompt™ inoculation		
			Manual	autoSCAN ®	Walk-Away®	Manual	autoSCAN ®	Walk-Away®
E. coli ATCC 25922 Expected range 2/1 – 8/4 ug/mL	1/0.5							
	2/1	2			9			4
	4/2	84	99	81	72	92	73	70
	8/4	26	13	1	1	19	7	6
	16/8							
						1	2	2
E. coli ATCC 35218 Expected range 4/2 – 16/8 ug/mL	2/1	2	4	2	2	4	1	1
	4/2	5	32	29	29	26	23	22
	8/4	83	60	37	37	68	45	46
	16/8	9	3	1	1	1		
	32/16							

Quality control results demonstrated the ability of all variables of the procedure (reading and inoculation) to produce acceptable results. There does not appear to be much of a trend in any of the methods, but the Prompt™ results were less reproducible than the turbidity method of inoculation for the *E. coli* STCC 25922.

Inoculum density control: A turbidity meter was used for the turbidity inoculation method. The Prompt™ method of inoculation had colony counts performed periodically throughout the study to determine the average inoculum density since there is no visual check of the inoculum using this device. Colony counts were also performed using the turbidity method when inoculating both the dried MicroScan® panels and the frozen reference panels. The turbidity method of inoculation for the reference test and all QC strains tested (n =83)had an average inoculum that was in the range of 3 X 10^5 to 4.6 X 10^5, while the Prompt™ method of inoculation had far more variability with average inoculum ranges from 5.4 to 14 X 10^5. The inoculum of the Prompt™ method of inoculation generally provides a higher number of CFU with more variability than a method using a turbidity meter. The chart below shows this comparison.

organism	Method of inoculation	Lowest CC x 10^5	Highest CC x 10^5	Average CC x 10^5
E. coli ATCC 25922	Prompt™	1.8	92	10.4
	Reference	1.1	4.9	3.8
E. coli ATCC 35218	Prompt™	3.2	36	9.6
	Reference	2.3	6.8	3.7

d. Detection limit:
Not applicable

e. Analytical specificity:
Not applicable

f. Assay cut-off:
Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Clinical testing was performed at three sites using mainly fresh isolates supplemented with stock isolates of *Enterobacteriaceae*. A comparison of the MicroScan® Dried Gram-Negative test panel results was made to the reference method conducted as recommended in the NCCLS standard M7-A6. Testing of the reference method and the MicroScan panels was performed at the same time. A challenge set was also tested

at one site and compared to the reference broth dilution result mode that was determined by previous testing of each isolate multiple times in the recommended reference panel.

Turbidity inoculum with manual readings.

	total	**EA**	**%EA**	**Total evaluable**	**EA of evaluable**	**%EA**	**CA**	**%CA**	**#R**	**min**	**maj**	**vmj**
Clinical	302	301	99.7	300	299	99.7	292	96.7	102	10	0	0
Challenge	75	75	100	73	73	100	71	94.7	30	4	0	0
Combined	377	376	99.7	373	372	99.7	363	96.3	132	14	0	0

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates
maj-major discrepancies
vmj-very major discrepancies
min- minor discrepancies

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within the plus/minus one well variability. EA is when there is agreement between the reference method and the MicroScan® within plus or minus one serial two-fold dilution of antibiotic. CA is when the interpretation of the reference method agrees exactly with the interpretation of the MicroScan® result.

The challenge set of organisms was also tested using the Prompt™ method of inoculation with all reading methods and the turbidity method of inoculation with the WalkAway® and the autoSCAN®4. This included seventy five challenge isolates that were tested at one site. The inoculum was prepared by the turbidity or Prompt™ method and incubated in the WalkAway® instrument. All panels had additional readings performed after the WalkAway® reading was completed using the autoSCAN®-4 and then manually on the touchSCAN®-SR.

The following table demonstrates the performance based on essential agreement and category agreement for the challenge set and the different inoculation and reading methods.

	total	EA	%EA	Total evaluable	EA of evaluable	%EA	CA	%CA	#R	min	maj	vmj
Turbidity/ manual	75	75	100	73	73	100	71	94.7	30	4	0	0
Turbidity/ WalkAway®	75	75	100	73	73	100	70	93.3	30	5	0	0
Turbidity/ autoSCAN®	75	75	100	73	73	100	70	93.3	30	5	0	0
Prompt™/ manual	75	74	98.7	73	73	100	71	94.7	30	4	0	0
Prompt™/ WalkAway®	75	74	98.7	73	73	100	70	93.3	30	4	0	1
Prompt™/ autoSCAN®	75	74	98.7	73	73	100	70	93.3	30	4	0	1

b. Matrix comparison:
Not applicable

3. Clinical studies:
   a. Clinical sensitivity:
   Not applicable
   b. Clinical specificity:
   Not applicable
   c. Other clinical supportive data (when a and b are not applicable):
   Not applicable
4. Clinical cut-off:
   Not applicable
5. Expected values/Reference range:
   ≤ 8/4 (S), 16/8 (I), ≥ 32/16 (R)
   The interpretative criteria and QC are the same as recommended in NCCLS. All values will be included in the package insert.

M. Conclusion:

The reproducibility, quality control results and overall performance is acceptable as described in the "Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA" which was used in the design and evaluation of the study. The appropriate control organisms are included in the labeling and are the same as those recommended in the NCCLS M7-(M100-S13) document. This performance as compared to a standard method demonstrates substantial equivalency to the predicate.